

**REMARKS**

The specification has been amended to reflect the 371 status.

In addition, the claims have been amended to remove the multiple dependencies, in order to eliminate the improper multiple dependencies and to reduce the PTO filing fee.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached pages are captioned "Version with markings to show changes made".

Favorable action on the merits is solicited.

Respectfully submitted,

Takaki WARITANI et al.

By Warren M. Cheek, Jr.  
Warren M. Cheek, Jr.  
Registration No. 33,367  
Attorney for Applicants

WMC/dlk  
Washington, D.C.  
Telephone (202) 721-8200  
Facsimile (202) 721-8250  
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MONOCLONAL ANTIBODY AGAINST CANINE TRYPSIN

*Ans a' →* ~~This application is a 371 of PCT/JP99/04299 Filed August 9, 1999.~~

BACKGROUND OF THE INVENTION

1. Technical Field of the Invention

The present invention relates to a monoclonal antibody (MAb) to canine trypsin or a substance related thereto, to an immunoassay for trypsin and/or trypsin-like immunoreactivity which comprises using the said MAb and to an immunoassay reagent for trypsin and/or trypsin-like immunoreactivity which comprises an effective amount of the said MAb. In another aspect, the present invention relates to a method for diagnosing a member selected from diseases and disorders including pancreas diseases such as acute pancreatitis, chronic pancreatitis, pancreatic cancer and exocrine pancreatic insufficiency, splanchnic diseases such as renal insufficiency, etc. which comprises using the said immunoassay reagent and/or the said immunoassay, and further to an agent for diagnosis thereof.

2. Description of Related Art

Trypsin is one of proteinases (proteolytic enzymes) occurring among various animals including human, dog, cat, bovine, horse, swine, sheep, goat, etc. and biosynthesized in a zymogen precursor, trypsinogen, by pancreatic acinous cells of the pancreas. Trypsinogen is secreted into the duodenum followed by conversion into the active form, trypsin, by the hydrolytic action of enterokinase or trypsin itself. Trypsin predominantly acts to digest dietary proteins in the intestine. Further, trypsin restrictively degrades other zymogen precursors including chymotrypsinogen, procarboxypeptidase, phospholipase, etc. to produce active form enzymes. It has been known that human trypsinogen includes two subtypes, i.e., cationic form (cationic trypsinogen) and anionic form

What is claimed is:

1. A monoclonal antibody against canine trypsin or a canine trypsin-related substance.

2. The monoclonal antibody according to Claim 1 which is an antibody to at least one member selected from the group consisting of canine cationic trypsinogen, canine anionic trypsinogen, canine cationic trypsin, canine anionic trypsin and canine trypsin-related substances derived therefrom.

3. The monoclonal antibody according to Claim 1 which is an antibody to at least one member selected from the group consisting of (a) a protein of SEQ ID NO: 1 or SEQ ID NO: 2 in the Sequence Listing, or a salt thereof and (b) a peptide fragment thereof, or a salt thereof.

*Claim 1* 4. The monoclonal antibody according to ~~any of claims 1 to 3~~ which is an antibody to at least one member selected from the group consisting of canine cationic trypsinogen, canine cationic trypsin, and canine cationic trypsin-related substance derived therefrom.

*Claim 1* 5. The monoclonal antibody according to ~~any of claims 1 to 3~~ which is an antibody to at least one member selected from the group consisting of

(1) a Thr<sup>16</sup> to Ser<sup>247</sup> amino acid sequence of SEQ ID NO:1 in the Sequence Listing,

(2) an Ile<sup>24</sup> to Ser<sup>247</sup> amino acid sequence of SEQ ID NO:1 in the Sequence Listing,

(3) a Phe<sup>16</sup> to Asn<sup>246</sup> amino acid sequence of SEQ ID NO:2 in the Sequence Listing, and

(4) an Ile<sup>24</sup> to Asn<sup>246</sup> amino acid sequence of SEQ ID NO:2 in the Sequence Listing.

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6. An immunoassay for trypsin and/or trypsin-like immunoreactivity (TLI) which comprises using an assay reagent containing the monoclonal antibody according to <sup>claim 1.</sup> ~~any of Claims 1 to 5.~~

7. The immunoassay according to Claim 6 wherein the trypsin-like immunoreactivity (TLI) is a member selected from the group consisting of trypsinogen, trypsin and their complexes with inhibitors.

8. An immunoassay reagent for trypsin and/or trypsin-like immunoreactivity (TLI) which comprises an effective amount of a monoclonal antibody according to <sup>Claim 1</sup> ~~any of Claims 1 to 5.~~

9. The immunoassay reagent according to Claim 8 wherein the trypsin-like immunoreactivity (TLI) is a member selected from the group consisting of trypsinogen, trypsin and their complexes with inhibitors.